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PRINCIPAL INVESTIGATOR: Seong K. Mun, Ph.D.

CONTRACTING ORGANIZATION: Georgetown University
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Seong K. Mun, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Georgetown University
Washington, DC 20057

E-Mail: Smun01@georgetown.edu

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The purpose of this study was to develop basic climatic and ecological profiling for the District of Columbia using ground meteorological and remotely sensed data provided by NOAA for transmission risk assessments for endemic and exotic mosquito-vectored pathogens. Key research pathogens. Key research outcomes:

- Successful compilation of ground meteorological and remotely sensed data provided by NOAA for the District of Columbia for an assessment of seasonal climatic and environmental change.
- Successful merging of enviro-climatic profiling with avian and mosquito collection data provided by the DC Department of Health (DOH) for use in delineating the seasonal changes in population densities. The merger of this data was produced within a Geographic Information System (GIS) mapping environment in partnership with the Utah State University GIS Program
- Provided a briefing in August 2003 to DC DOH public health officers in the use of meteorological and remotely sensed data for future analyses. Established a permanent, ongoing collaboration for biosurveillance system development in the District.
- Initial development of the first data security matrix for integrated biodefense that objectively places RSEPIS within the proper context for management of data sources

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4 Introduction

In 1999, West Nile (WN) fever, a mosquito-transmitted viral infectious disease, was identified for the first time in the Western Hemisphere in New York City (NYC). This was an unprecedented event, as West Nile Virus (WNV) had been considered endemic to the Middle East, Africa, and Asia. The first human cases of this outbreak were identified on August 2, 1999, with additional cases reported until September 22, 1999. Investigators retrospectively identified 61 human cases, 55 of which were hospitalized with infection involving brain tissue ("meningo-encephalitis"), resulting in 7 deaths. Further investigation revealed that a WN epidemic in birds had preceded the human phase of the epidemic by nearly a month. Furthermore, the virus was found to be capable of over-wintering in local mosquitoes and thus had gained permanent ecological establishment.[1-8]

The transmission cycle of WNV is complicated. An amplification cycle is the initial event where bird-preferential mosquito vectors (e.g., *Culex* species) transmit the virus within local avian populations. Once the amplification cycle has started, bridging mosquito vectors (e.g., *Aedes albopictus*) feed on infected birds and then bite animals and humans, and so infect them. In humans, the vast majority of West Nile cases present as a mild viral illness. In some patients older than 55 years of age, the virus has a higher tendency to infect the brain, with associated higher death rates. Presently, there is no cure and no vaccine. Preventive measures include spraying for mosquitoes and wearing long sleeved shirts and insect repellent.

West Nile fever was not the first introduction of exotic infectious disease to the United States and is not anticipated to be the last with air travel to the US from foreign origins anticipated to steadily increase. Analyses performed by the US Department of Transportation in 1998 showed over 200 million people entering the US by airflight over a four-year period. The most rapidly developing regional air traffic markets were found to be the same areas of major concern to the US Centers for Disease Control and Prevention and the World Health Organization for foreign infectious disease control. In the post-9/11 environment, the US remains as ever-increasing risk for deliberate introduction of an exotic pathogen by a terrorist, with the potential for ecological establishment. Overall risk for future novel appearances of exotic pathogens, either via accidental or deliberate means, in the US has steadily increased.[9, 10]

Basic understanding of local urban climatology and ecology is key to assessing risk for epidemic triggering once a case of an exotic insect-transmissible infectious disease is identified. For each US city, several species of mosquitoes are present in population distributions that vary depending on the season, climatologic factors, and local ecology. These mosquitoes have varying capacities to transmit known, US-endemic pathogens. As demonstrated by the West Nile epidemic, local mosquitoes are also transmission-competent for multiple exotic pathogens and subject to modulation by enviro-climatic conditions.[11]

The advent of more sophisticated instrumentation onboard satellites placed in orbit by the National Oceanic and Atmospheric Administration (NOAA), in conjunction with meteorologic data provided by the NOAA National Weather Service, offered new opportunities to study local urban ecology and links between seasonal changes in mosquito population densities and climatic modulation, or changes in the local meteorologic environment of a city. Awareness of monthly-anticipated mosquito population densities, aggregated by species and transmission competencies for both endemic and exotic pathogens, becomes an important tool for understanding risk for epidemic triggering, propagation, and possible ecologic establishment. Had West Nile virus been introduced at a time when the mosquito counts were low, either due to disruption of the anticipated seasonal bloom or lack of appropriate conditions to favor mosquito population expansion, an epidemic may not have been triggered.

The purpose of this study was to develop basic climatic and ecological profiling for the District of Colombia using ground meteorological and remotely sensed data provided by NOAA for transmission risk assessments for endemic and exotic mosquito-vectored pathogens.

5 Report Body

This section describes the research accomplishments associated research performed from 1 September 2002 to 31 August 2003. The award number is DAMD17-94-V-4015.

5.1 US Analysis

In 2002, 4,156 human cases of WN fever were identified in the US, with 284 deaths.[3] This was the largest insect-vectored meningo-encephalitis epidemic in the known history of the Western Hemisphere and the largest WNV-related meningo-encephalitis epidemic worldwide recorded to-date. Ecological damage has been an unforeseen consequence, with over 140 species of birds, reptiles, and mammals have been infected and killed by WNV in the US, and over 36 species of mosquitoes are known to be able to transmit the virus. Over 14,000 horses were killed due to WNV since the epidemic began in 1999. West Nile virus has also posed a major threat to endangered species and zoological park animals, with over 100 US zoos reporting cases.[4, 8] The spread of WNV is exemplified by the choropleth maps of the US as shown in Figure 1 (a and b).[3]

First Appearance of West Nile Virus in Birds, Mosquitoes, and other Animals by Year

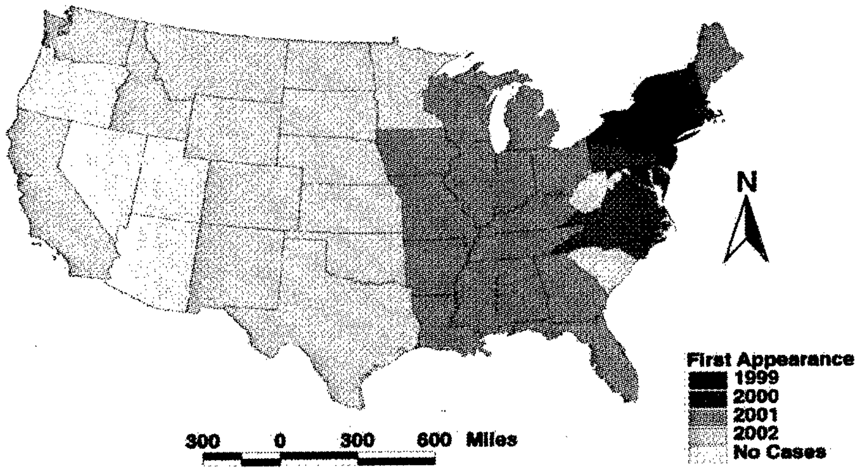


Figure 1a: Spread of WNV in birds, mosquitoes, and other animals since 1999. The initial North-South spread along the East Cost can be explained by migratory pathways of birds. One possible explanation for the quick spread of WNV from the East to the West can be the incidental transportation of infected mosquitoes via air and terrestrial transportation.

First Appearance of West Nile Virus in Humans by Year

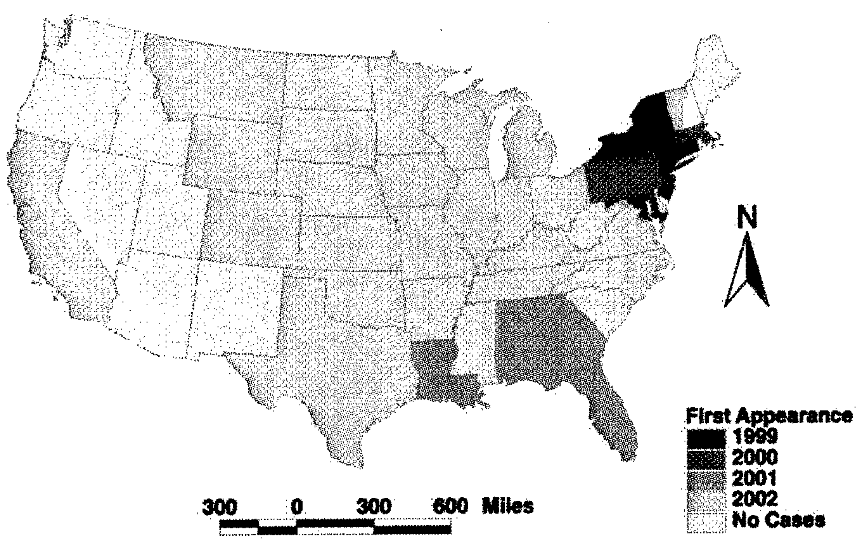


Figure 1b: Spread of WNV in humans since 1999. The first appearance of WNV in humans in a state usually lags the appearance of WNV in birds, mosquitoes, and other animals by a few months up to 1 to 2 years. By the end of 2002, only 11 states had no human WN cases.

Figure 2a, a similar representation as Figures 1a and 1b showing infection rate by state, demonstrates the limitation of choropleth representations. Referenced to Figure 2b, however, micromap representation of the same data illustrates higher infection rates in the Midwest, a conclusion that would be difficult to come by using Figure 2a by itself. Of note, in Figure 2b is the high national profile of DC in respect to infection rate.

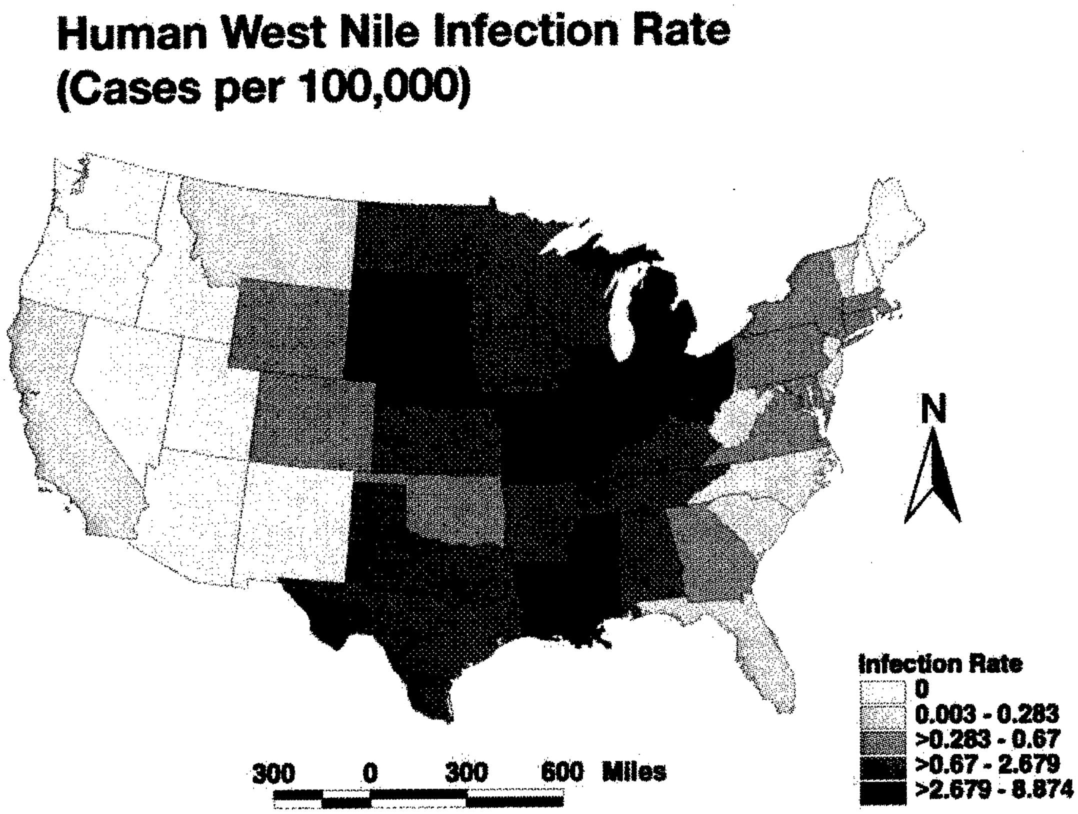


Figure 2a: Human WN infection rates by state based on data sources from CDC and the US Census Bureau. Highest rates were observed in the central states. Due to lack of available data, the rates on this map were not age adjusted.

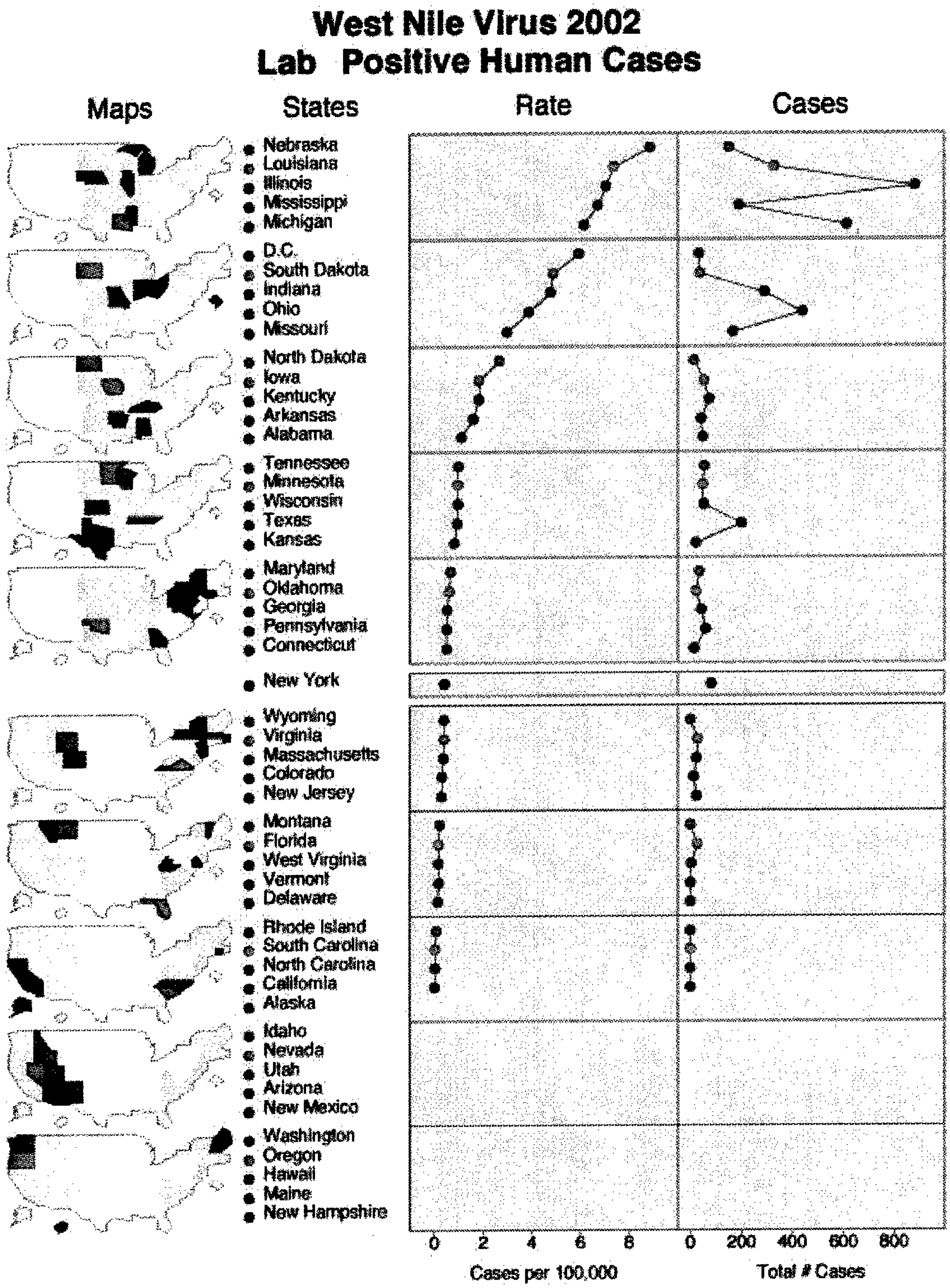


Figure 2b: Linked micromap plots showing the same WN infection rates (as Figure 3a) and total number of human WN cases for states. The micromap plots highlight spatial structures (highest WN rates in the central states, lowest WN rates along the East Coast), spatial outliers (notable DC), and regions commonly overlooked when referencing a choropleth representation as in Figure 2a- i.e., Nebraska, with only 152 cases, but with the highest WN infection rate. No WN cases have been observed in 2002 in the eleven states listed at the bottom. New York has the median WN infection rate.

5.2 DC Analysis

The first evidence of WNV in the District of Columbia was documented in 2000 with the discovery of 5 WNV positive birds; this number increased to 360 in 2001 with the discovery of 3 positive pools of vector mosquitoes and no animal or human cases. In 2002, the first positive bird was identified on May 2nd, first positive mosquito vectors were found in July, and the first human case was infected in late July. Full ecological establishment of WNV in the District of Columbia was established in 2002.[10]

For future reference, Figure 3 is a representative map of the Washington, DC area highlighting the eight wards that comprise the administrative units. In addition, both woodland and water bodies are identified for reference, along with the cooperative weather stations (COOP). Data from the COOP stations were part of the enviro-climatic analysis for the DC area.

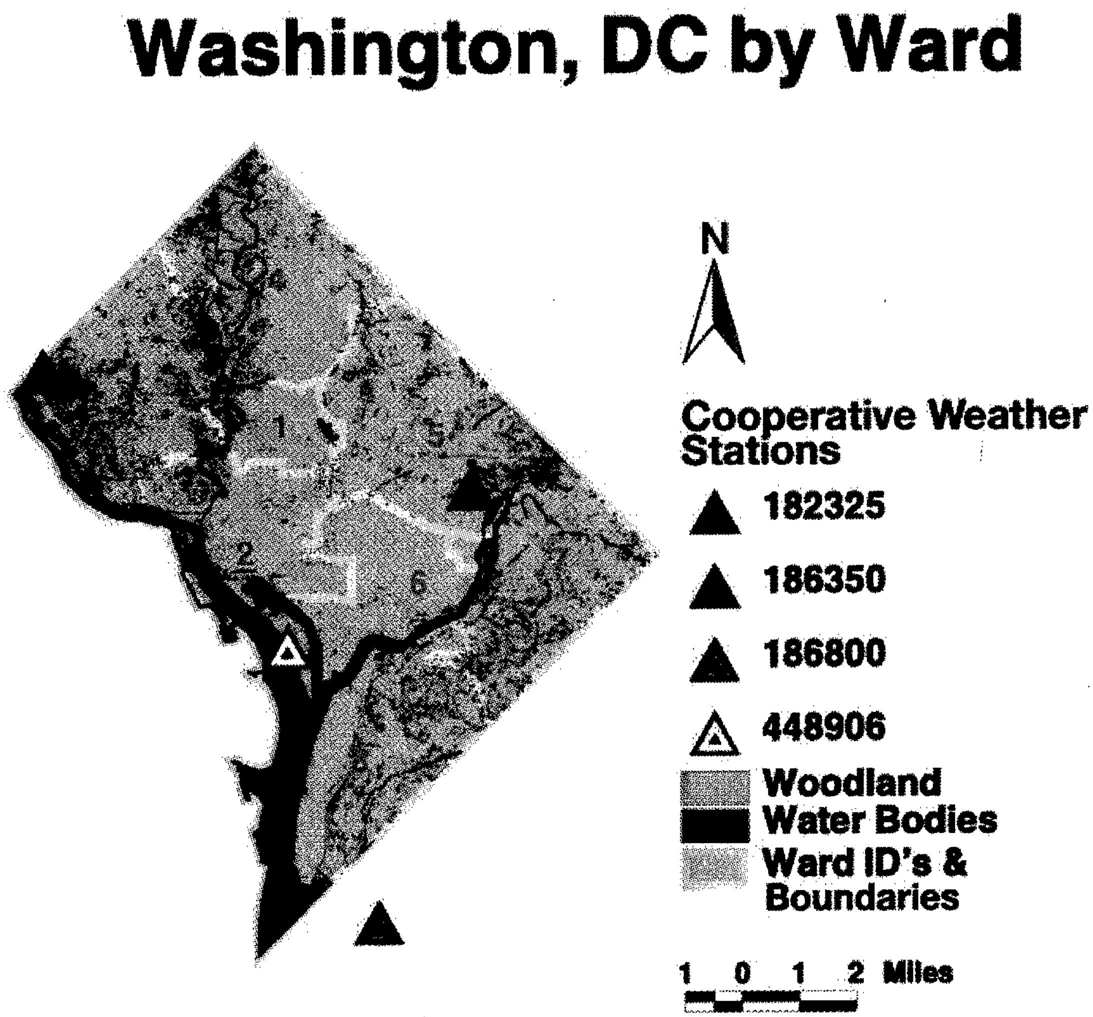


Figure 3: Washington DC map, highlighting administrative units (wards), woodland areas and water bodies, and COOP weather stations used.

An analysis for DC similar to that for the US is portrayed in Figures 4a and 4b. Figure 4a is quite striking in that it shows that Ward 3 is associated with a ten-fold elevation in WNV-infected birds as compared to the next highest ward. Figure 4b, number of WNV cases in humans, mirrors the statistics for Ward 3 in that the highest number of human cases occurs in this ward. A further analysis of DC is given by a geographic time series representation of the weekly mosquito WNV-positive rates (Figure 4c). Note that Ward 3 again stands out as an area of high levels of infection. This provides the same information as a choropleth map; however this visualization provides the added benefit of noting the timing of mosquito positive rates reaching a critical value. Figures 4a and b could be shown in a similar manner, and they would show progression of the disease as would be expected (i.e., birds, then mosquitoes, then humans).

Total Number of WN Infected Dead Birds by Ward in DC for 2002

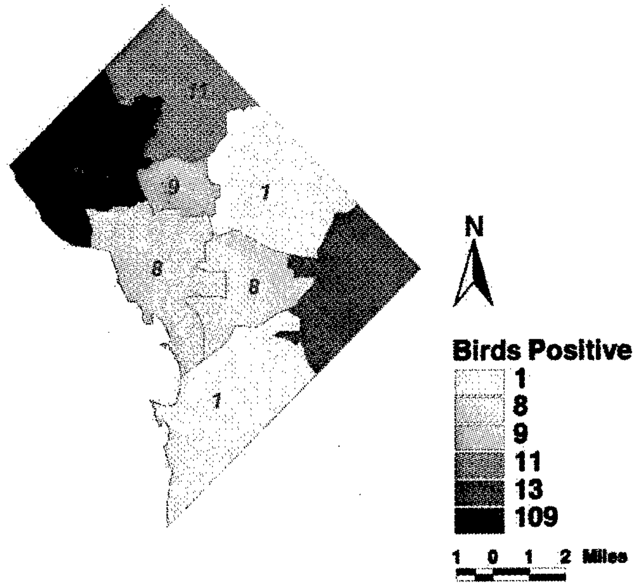


Figure 4a: Total number of WN infected dead birds in DC in the summer of 2002. The highest number was found in Ward 2. The map is based on a convenience sample based on people reporting dead birds. Moreover, only about 75% of reported dead birds could be tested for WNV.

Total Number of West Nile Cases in Humans by Ward in DC for 2002

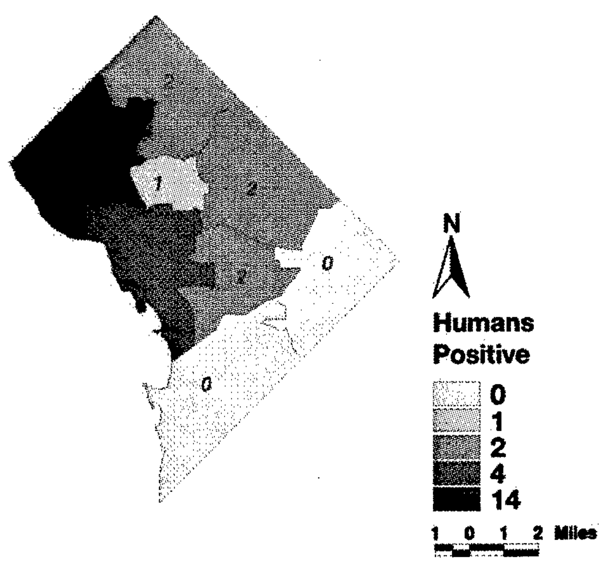
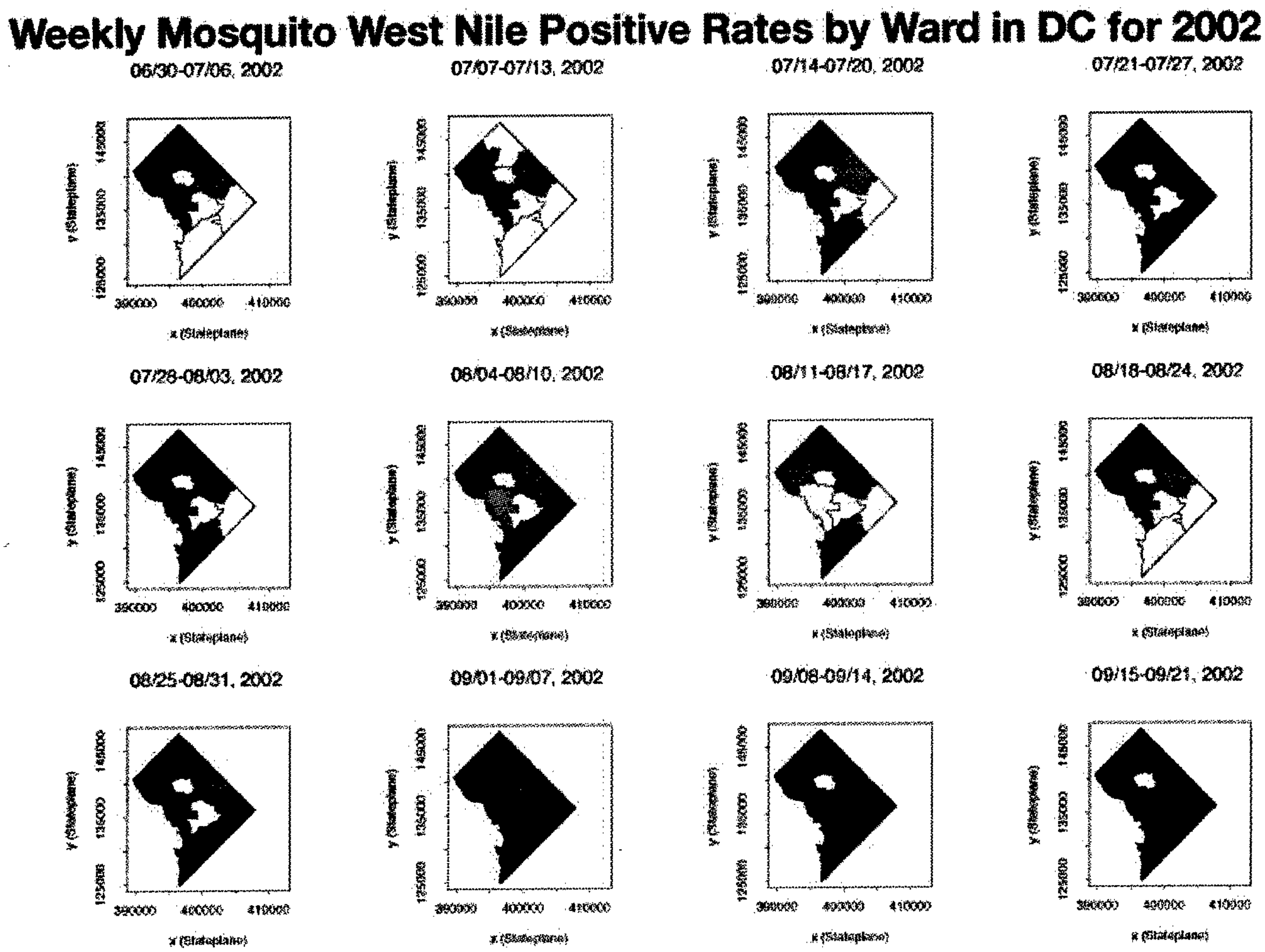


Figure 4b: Total number of WN infections in humans in DC in the summer of 2002. Similar to the bird WN infections in Figure 5a, the highest number was found in Ward 3. The total number of human cases reported in this map is less than the number for DC in figures 3a and 3b. Some of the human cases initially reported turned out to be WN negative.



<u>Figure 4c</u>: Geographic time-series of the spread of WN in mosquitoes in the summer of 2002. Red is used to display regions where sampled pools of mosquitoes tested positive. The brighter red, the higher the percentage of positive sampled pools. The brightest red used, for example, in week 8/4 – 8/10 for Ward 2 where 42% of the sampled pools (11 out of 26) tested positive. Green is used to display regions where all sampled pools of mosquitoes tested negative. The brighter green, the higher the number of negative sampled. The brightest green is used in week 8/4 – 8/10 for Ward 4, where all 33 sampled pools tested negative.

A further analysis of the enviro-climatic set is given in Figure 5, panels a to c. The spring seasonal transition in the DC area was noted based on air temperature and remotely sensed Normalized Difference Vegetation Index (NDVI) data: NDVI being an indicator of vegetation cover over the ground. The minor rainy season (panel b) in the District from March to June likely contributed to hydration and subsequent hatching of mosquito eggs. Of note was the observation of a temperature and NDVI peak over July and August. This is an important observation because the ability of a mosquito to transmit WNV is maximized with increases in temperature, specifically 26 to 30 degrees Centigrade. And such high temperatures occurred within the time frame of infection as observed in the bird, mosquito, and human analyses provided earlier. We believe the discovery of positive mosquitoes followed by positive human cases in July, August, and September is directly related to this temperature increase and raises important implications for future mosquito control efforts in the District. The NDVI analysis is supportive in the sense that it is driven by the climate (particularly temperature). Whereas temperature is a point measurement of which there are a few stations in the DC area (ref: Figure 3). NDVI is a spatially distributed variable that reflects the spatial complexity of the temperature data more fully. Definition of environment competency to sustain transmission using satellite imagery-derived NDVI implied a potential for use as a Remotely Sensed Epidemic Surveillance (RSEPIS) system to identify "conditions favorable" for epidemic transmission.

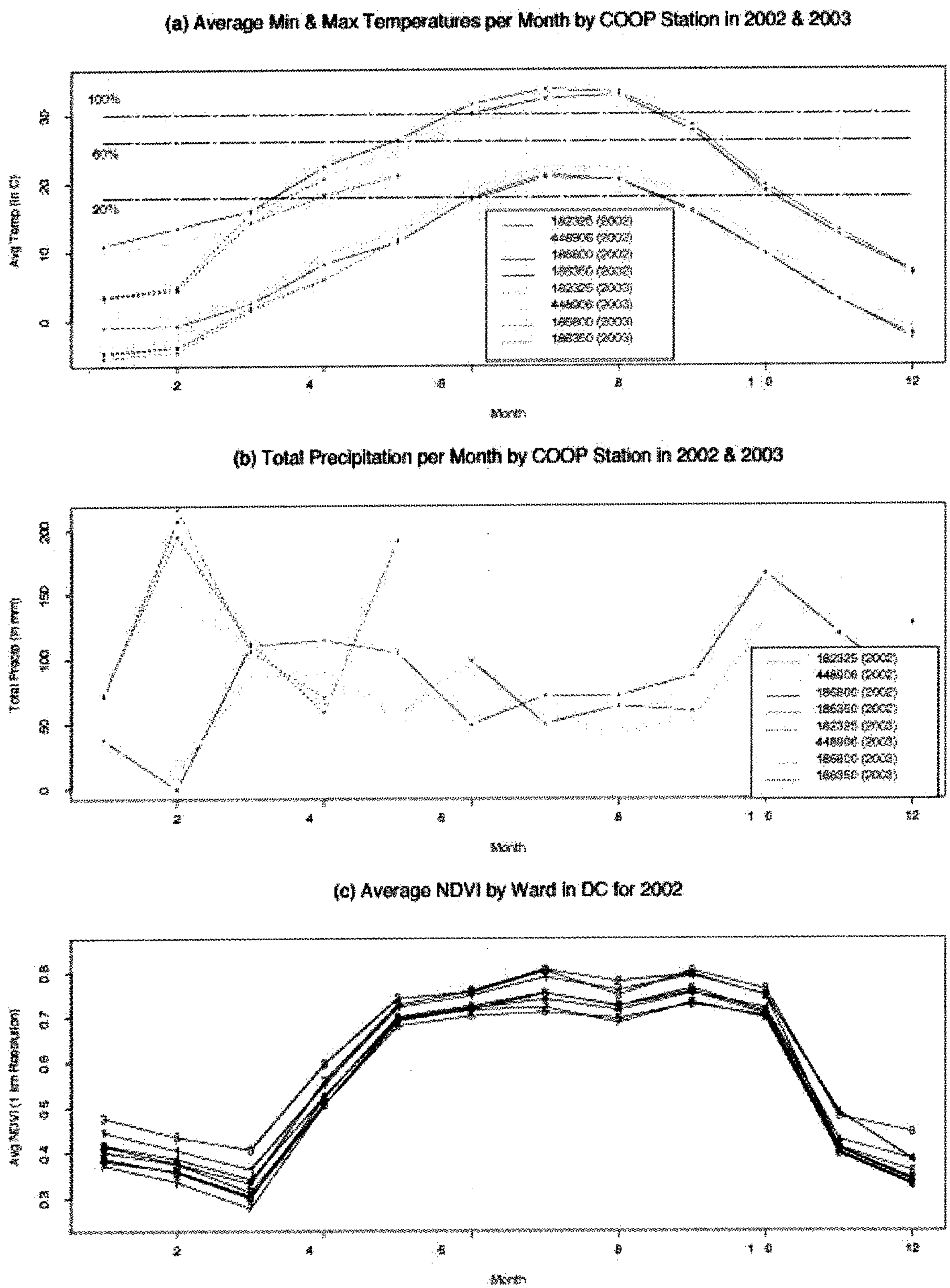
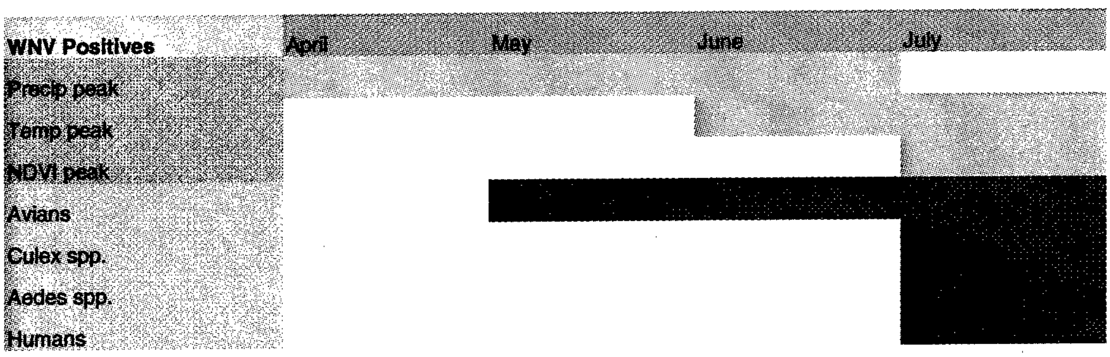


Figure 5: (a) Average min / max temperatures per month, revealing a continuous increase of temperatures from January through July/August. The 2003 min / max temperatures are consistently lower than the 2002 temperatures for the same time period (until May 2003). No further 2003 data is available yet. The dotted percentage lines indicate transmission competency of *Culex pipiens* for WNV based on laboratory data provided by Mike Turell, US Army Medical

Research Institute for Infectious Disease. A higher percentage indicates a higher efficiency of the mosquito to transmit the virus.
(b) Total precipitation per month for the entire year of 2002 and part of 2003. There is consistent precipitation each month while the monthly precipitation data for 2003 is markedly higher as far as the record goes.
(c) Average Normalized Vegetation Index (NDVI) by ward for 2002. The average is computed from the second 10 month composite of SPOT reflectance data. The data is consistent with seasonal green-up and green-down and shows that for certain wards (e.g., Ward 3) the green-up is more elevated, hence the possible establishment of more expansive mosquito breeding habits.

The final concept developed in Phase I was the creation of a matrix of Indications and Warnings (I&Ws) for the full ecological establishment of WNV in the District of Columbia referred to as "Graded Alerting", shown in Figure 6.



<u>Figure 6</u>: "Graded Alerting" matrix for Indications and Warnings (I&Ws) of imminent WN transmission in humans. In the left column are I&Ws relevant to WNV. The green and blue bars extending from April to July mark the time point at which each I&W appeared in the DC area.

Imminence of human exposures is implied by the combination of I&Ws observed. Precipitation peak with WNV-positive birds appearing in April to May represents a low risk time period with up to 4 weeks of time to highest probability of human infection. Precipitation and temperature peaking with WNV-positive birds in May to June implies an immediate level of risk with weeks of lead-time. Peaking of NDVI values following appropriate increases in precipitation and temperature with WNV-positive birds and mosquitoes in June to July implies immediate threat with days of lead-time. Graded Alerting attempts to place into context the importance of data sources that yield the I&W in question, from ground meteorological and remotely sensed date to bird, mosquito, animal, and human surveillance data. The technique of Graded Alerting can provide support to decision makers attempting to implement a response plan to the novel appearance of an exotic zoonotic bioagent. Graded Alerting will require ongoing testing and validation in Phase II.

Given the implications to national biosecurity, the Vanguard Phase I RSEPIS prototype and Graded Alerting concept were evaluated within the context of other data sources under investigation by ISIS Biodefense to implement a management plan that ensures adequate data security, as shown in Figure 7.

I&W Description			Source		ISIS	
Category	Type	Subtype	MAC	Confidentiality	MAC	Confidentiality
Direct Disease Surveillance	PHI	Raw	III	Sensitive	I	Sensitive
		Processed	III	Sensitive	I	Sensitive
	Companion animals	Raw	III	Sensitive	I	Sensitive
		Processed	III	Sensitive	I	Sensitive
	Zoological animals	Raw	III	Sensitive	I	Sensitive
		Processed	III	Sensitive	I	Sensitive
	Free-ranging wildlife	Raw	III	Sensitive	I	Sensitive
		Processed	III	Sensitive	I	Sensitive
	Food animals	Raw	n/a	n/a	n/a	n/a
		Processed	III	Sensitive	I	Sensitive
	Plant/crops	Raw	n/a	n/a	n/a	n/a
		Processed	III	Sensitive	II	Sensitive
	Vector surveillance	Raw	III	Sensitive	II	Sensitive
		Processed	III	Sensitive	II	Sensitive
Socio-Economic Markers	Telecomm use	Raw	I	Sensitive	I	Sensitive
		Processed	I	Sensitive	I	Sensitive
	Internet use	Raw	n/a	n/a	n/a	n/a
		Processed	III	Sensitive	II	Sensitive
	Transportation	Raw	I	Sensitive	n/a	n/a
		Processed	III	Sensitive	I	Sensitive
	Credit/debit/discount card use	Raw	III	Sensitive	II	Sensitive
		Processed	III	Sensitive	II	Sensitive
	Media tracking	Raw	III	Open	I	Sensitive
		Processed	III	Open	I	Sensitive
	Infrastructure closings (e.g., schools)	Raw	III	Open	I	Sensitive
		Processed	III	Open	I	Sensitive
	Pharmaceutical sales	Raw	n/a	n/a	n/a	n/a
		Processed	III	Sensitive	II	Sensitive
Chain of Evidence	FDA product recall events	Raw	n/a	n/a	n/a	n/a
		Processed	III	Open	II	Open
	Vaccine contaminations/events	Raw	n/a	n/a	n/a	n/a
		Processed	III	Sensitive	II	Sensitive
	Pharmaceutical contamination/events	Raw	n/a	n/a	n/a	n/a
		Processed	III	Sensitive	II	Sensitive
	Water contamination events	Raw	n/a	n/a	n/a	n/a
		Processed	III	Sensitive	II	Sensitive
Enviro-Climatic Indices	Ground meteorology	Raw	III	Open	I	Sensitive
		Processed	III	Open	I	Sensitive
	Remote sensing	Raw	III	Open	II	Sensitive
		Processed	III	Open	II	Sensitive

Figure 7: Data Security Matrix for Integrated Biosurveillance. Confidentiality Level refers to whether the data is considered classified, sensitive, or open. Mission Assurance Category (MAC) defines the data availability and criticality. Both the Confidentiality Level and MAC may be different depending on the perspective of the source or within the biosurveillance environment at ISIS.

The Data Security Matrix for Integrated Biosurveillance has become the framework for broader I&W development in surveillance for catastrophic bioevents. Development of the Biosecurity Matrix was initiated within Project Vanguard Phase I.

5.3 Phase II Plans

As shown in Figure 7, WNV has spread from the East Coast towards the West. Although positive identification of WNV has been documented in California, it has not been identified in the state of Utah.

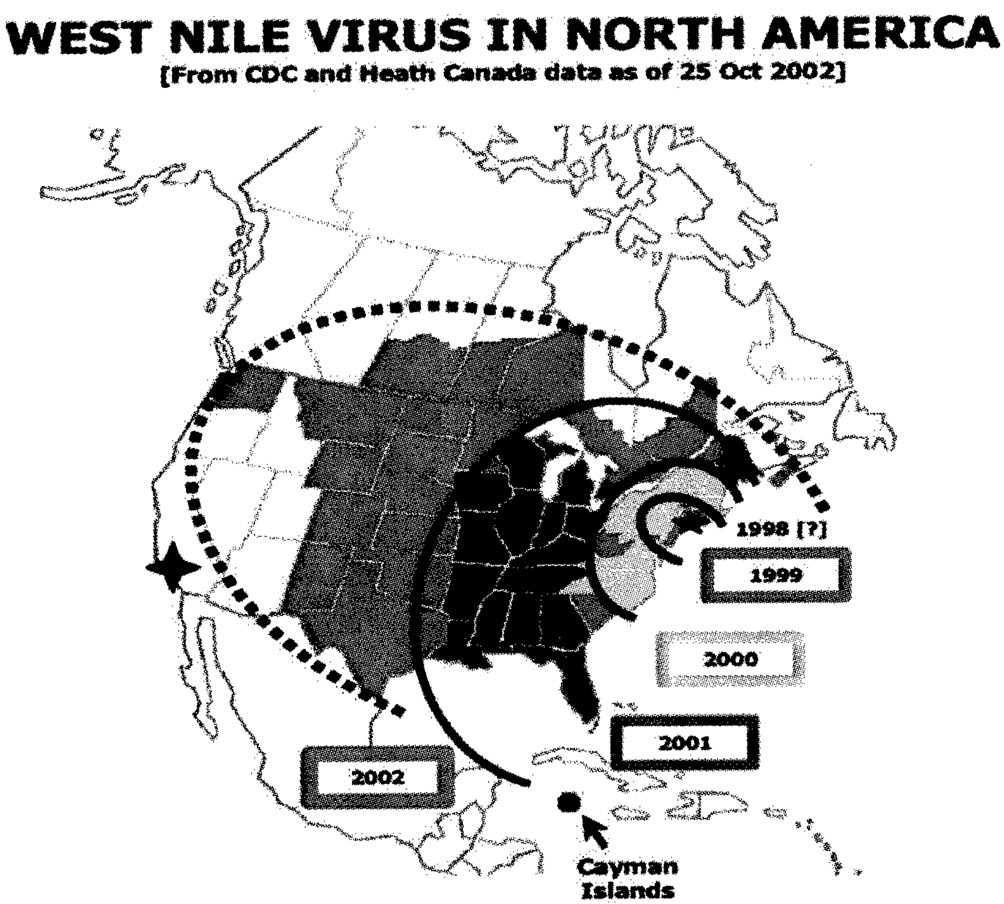


Figure 7: WNV in North America (1999-2002). Credit: Joseph Dudley, PhD, U.S. Army Environmental Programs Directorate, Versar, Inc., CDC and USAMRIID

The Utah State Department of Health (DOH) is actively screening mosquito collections and animal and human serologies for evidence of WNV infection. WNV was anticipated to gain ecological establishment in 2003.

Given the lower degree of urbanization and higher percentage of the local economy devoted to agriculture, the Cache Valley (northeast of Salt Lake City) offers a unique mirror site to Vanguard I-Washington, DC whereby an urban model for WNV

transmission can be compared to a rural model. It is important for RSEPIS applications to include animal and agricultural concerns for more comprehensive application to homeland biosecurity.

A WNV workshop was held at Logan Utah on Dec 3rd 2002 involving representatives of Utah State University, the State of Utah, Bronx Zoo, Georgetown University and USAMRID. The growing concerns for the animals and wild life were expressed by the experts and need to look at rural communities were emphasized. The meeting reflected the urgency and importance for the rural impact of WNV.

On July 15th, 2003, ISIS and the University of Maryland sponsored the "Comprehensive Modeling of the Introduction of West Nile Virus (WNV) to the United States as a Proxy to Intentional Mosquito-Vectored Bioagent Release Workshop", which created a multiple academic, private, and government partnership. This multi-disciplinary team couples WNV disease experts with disease modelers that have GIS visualization and spatial statistics expertise. The conclusion of these proceedings unanimously recognized the growing threat to national security that infectious diseases represent and declared the need for a seamless integrated biosurveillance system to enable ongoing studies such as Vanguard Phase I. Project Vanguard has served as a driver to enhance IT infrastructure to support robust biosurveillance, with an emphasis to advance the science of Indications and Warnings (I&Ws) for biological catastrophic events.

While Phase I Project dealt primarily with medical and public health issues in an urban area, Phase II includes farm and wild life animals in a rural region.

Objectives for Phase II:

The purpose of Phase II is to utilize IT to integrate the activities of multiple scientific disciplines to develop a prototype RSEPIS and Graded Alerting system for vectorborne infectious diseases in the Cache Valley, Utah. Development of an RSEPIS system depends on a comprehensive analysis of enviro-climatic coupling to infectious disease incidence. This investigation will use WNV as the test scenario and draw upon multiple disparate sources of data to evaluate the role of enviro-climatic modulation of WNV-transmission competent mosquito vectors in Cache Valley.

The fundamental scientific question to be addressed is:

- Can enviro-climatological models be developed that describe the relationship between mosquitoes, seasonal changes, and level of risk for transmission of WNV in **both urban and rural areas**?

Project Vanguard Phase II builds on prior experience by this collaborative and will access, analyze, and integrate data produced by different scientific disciplines for a synergistic result of new knowledge and tools developed for use in public health and homeland security applications.

The proposed research has the following specific aims:

Aim 1: Expand database for RSEPIS to include data elements relevant to Utah and integrate query mechanisms.
Aim 2: Apply the RSEPIS system to conventional West Nile epidemic surveillance in the Cache Valley, Utah area.

Additional Aims added to the scope of Phase II based on unforeseen novel discoveries in Phase I:

Aim 3: Evaluation and ongoing validation of the Graded Alerting concept.
Aim 4: Further development and implementation of the Biosecurity Data Management Matrix.

Phase II will compare the enviro-climatic-disease coupling model developed for the District to the rural environment of the Cache Valley, as well as the applicability of the RSEPIS prototype developed to rural environments. Ultimately, this will contribute to national awareness and understanding of US vulnerability to ecological establishment of exotic mosquito-vectored pathogens.

6 Key Research Outcomes

- Successful compilation of ground meteorological and remotely sensed data provided by NOAA for the District of Colombia for an assessment of seasonal climatic and environmental change.
- Successful merging of enviro-climatic profiling with avian and mosquito collection data provided by the DC Department of Health (DOH) for use in delineating the seasonal changes in population densities. The merger of this data was produced within a Geographic Information System (GIS) mapping environment in partnership with the Utah State University GIS Program.
- Provided a briefing in August 2003 to DC DOH public health officers in the use of meteorological and remotely sensed data for future analyses. Established a permanent, ongoing collaboration for biosurveillance system development in the District.
- Initial development of the first data security matrix for integrated biodefense, that objectively places RSEPIS within the proper context for management of data sources key to national biosurveillance.

7 Reportable Outcomes

- Developed first model of enviro-climatic-disease coupling model for WNV, as it pertains to the urban environment of the District of Columbia, that proposes enhancer and inhibitor enviro-climatic conditions that relate to WN transmission.
- Developed first prototype RSEPIS system for WNV in the DC area to highlight geotemporal "conditions favorable" for vectorborne transmission.

- Direct model relevance to the concern of epidemic trigger potential of Rift Valley fever should it be introduced to the DC area.
- Developed first proposed integrated "Graded Alerting" system for bioevents.
- Developed first data security matrix for integrated biosurveillance.

The findings of Project Vanguard Phase I will be submitted for publication in 2004.

8 Conclusions

It has been shown that WNV, a spatially and temporally complex phenomenon, can be described well and summarized using statistical visualization techniques. Here we have shown various representations of the data that have provided insight into the spread and ecological establishment of WNV, with implications for Rift Valley fever virus.

RSEPIS and Graded Alerting prototyping was demonstrated to have great potential utility to identify, geotemporally, areas of intense WN transmission. This is a potential source of proactive information, and Project Vanguard has provided the District of Columbia valuable information to guide their surveillance and response efforts for WNV. Ultimately, Project Vanguard has played an important role in defining requirements for integrated biosurveillance systems for national biodefense.

9 References

1. Nash D, Mostashari F, Fine A, Miller J, O'Leary D, Murray K, Huang A, Rosenberg A, Greenberg A, Sherman M, Wong S, and Layton M, 2001. The outbreak of West Nile virus infection in the New York City area in 1999. New England Journal of Medicine; 3441:1807-1814.
2. CDC, 2000. Notice to Readers: Update: West Nile Virus Isolated from Mosquitoes—New York, 2000. Morbidity and Mortality Weekly Report (MMWR) Mar 17, 2000;49(10):211. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm4910a4.htm
3. CDC, 2002. http://www.cdc.gov/od/oc/media/wncount.htm
4. CDC, 2002. Provisional Surveillance Summary of the West Nile Virus Epidemic --- United States, January--November 2002. Morbidity and Mortality Weekly Report (MMWR) December 20, 2002 / 51(50); 1129-1133. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5150a1.htm
5. CDC, 2002. Public Health Dispatch: Investigations of West Nile Virus Infections in Recipients of Blood Transfusions. Morbidity and Mortality Weekly Report (MMWR) October 25, 2002 / 51(42);973-974. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5137a5.htm
6. CDC, 2002. Possible West Nile Virus Transmission to an Infant Through Breast-Feeding --- Michigan, 2002. Morbidity and Mortality Weekly Report (MMWR) October 4, 2002 / 51(39); 877-878. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5139a1.htm
7. CDC, 2002. Intrauterine West Nile Virus Infection --- New York, 2002. Morbidity and Mortality Weekly Report (MMWR) December 20, 2002 / 51(50); 1135-1136. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5150a3.htm
8. ProMED, 2003. PRO/AH> West Nile virus update 2003 - USA (01), Archive Number 20030103.0016, Published Date 1/3/03. http://www.promedmail.org/pls/askus/f?p=2400:1001:527527::NO::F2400_P1001_BACK_PAGE,F2400_P1001_PUB_MAIL_ID:1000,20261

9. Office of Airline Statistics, 1998. US International air passenger and freight statistics (1994-1997). U.S. Department of Transportation, Washington, DC.
10. Lanciotti RS, Roehrig JT, Deubel V, Smith J, Parker M, Steele K, Crise B, Volpe KE, Crabtree MB, Scherret JH, Hall RA, MacKenzie JS, Cropp CB, Panigrahy B, Ostlund E, Schmitt B, Malkinson M, Banet C, Weissman J, Komar N, Savage HM, Stone W, McNamara T, Gubler DJ. Origin of the West Nile virus responsible for an outbreak of encephalitis in the northeastern United States. Science. 1999 Dec 17; 286(5448):2333-7. http://www.sciencemag.org/cgi/content/full/286/5448/2333
11. Brubaker JF and Turell MJ, 1998. Effect of environmental temperature on the susceptibility of *Culex pipiens* (Diptera: Culicidae) to Rift Valley fever virus. J Med Entomol. 1998 Nov;35(6):918-21.
12. DC DOH, 2003. West Nile Virus and Malaria Update. http://dchealth.dc.gov/information/wnv/wnv&malaria_update110402.shtm#program_overview